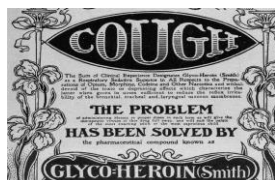


Edison Explains



Opioids

Why is the US in the middle of a devastating opioid crisis?



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The opioid epidemic, which is mired in a history of lax

regulation and permissive attitudes to pain relief, has troubled the US for decades.

The epidemic began with the adoption of opioids in end-of-life cancer patients. It expanded throughout the American Civil War with the use of opioids to treat soldiers intravenously, leading to the first major epidemic of addiction.

The epidemic was made worse by Felix Hoffmann, who re-synthesised diamorphine in the late 1890s. The company he worked for, and which went on to become Bayer, named the new drug heroin because it made the user feel 'heroic'.

The company now known as Bayer Pharmaceuticals continued a widespread trend of aggressive marketing for pain relief with its new drug, in what remains a poorly regulated US market.

More than 100 years later, opioid use accelerated as new cultural norms of pain management were established. The American Pain Society successfully campaigned in 1996 for the establishment of pain as the 'fifth vital sign'.

In 2004 the Federation of State Medical Boards claimed that 'physicians should recognize that tolerance and physical dependence are normal consequences of sustained use of opioid analgesics and are not the same as addiction'.

How has the opioid crisis worsened in the 21st century?

The cultural attitudes towards pain relief established in the late 1990s were unintentionally worsened by the 2006 Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey. The survey's scores

affected how hospitals were reimbursed by the government for Medicare and Medicaid services.

One of the three questions in the survey was 'How often did hospital staff do everything they could to help you with your pain?'

The survey's effects were magnified by the Affordable Care Act in 2010 ('Obamacare'), which used the same survey to help calculate reimbursements. The survey effectively sanctioned financial incentives for hospitals and doctors to prescribe opioids.

However, the American Pain Society's policy of pain as the fifth vital sign was reversed 2016. In addition, the questions in the HCAHPS survey relating to pain were amended in January 2018, but much of the damage was already done.

How extensive is the opioid epidemic?

The US suffered its third consecutive decline in life expectancy in 2017, mostly due to lethal opioid overdoses. Overdose is now the most common cause of death for those over the age of 50 in the US.

The Centers for Disease Control and Prevention (CDC) estimates that the opioid burden cost the US \$78.5bn a year and that 70,237 Americans died from overdoses in 2017, more than 47,000 of which were from opioids.

The European Monitoring Centre for Drugs and Drug Addiction estimates the total number of lethal overdoses in the EU-28, plus Turkey and Norway, at around 9,000 for 2016.

In the US there were nearly as many confirmed lethal overdoses in 2017 alone than the EU reported for the first decade of the 21st century. The EU has a population of roughly 513 million people. There are 328 million people in North America.

There were signs that the overdose death rate levelled off in 2018, but it is difficult to overstate the extent of the epidemic.

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'While the opioid epidemic is now widely-recognised, its commercial ramifications will linger for decades. This is because very few patients are cured but, as with other chronic indications, suffer relapses that also require medication-assisted treatment (MAT). Therefore, there continues to be an active need for products like Orexo's Zubsolv and new treatments for pain and opioid overdose.' Andy Smith, Analyst

How do opioids work?

Opioids bind with opioid receptors, most notably mu, delta, and kappa receptors. These receptors are present throughout the body and release a complex set of chemicals including endorphins – natural chemicals that regulate pain during and after exercise or food – and create a natural high. The effects are relief from pain and a feeling of euphoria.

The major burden of opioid dependence is tolerance, which leads to increased dosing. Each time opioids are used, the receptors become desensitized, leading to reduced neuronal cell excitability. Effectively, the body no longer releases endorphins and other chemicals, creating severe withdrawal symptoms that are particularly dangerous and difficult to resist.

How is opioid addiction treated?

In addition to psychiatric care, a few pharmacological treatments are available for those suffering from opioid addiction. The most common drug is methadone, a mu-opioid receptor agonist with a long duration of action. It can reduce the effect of opioid withdrawal while blocking the feeling of euphoria.

During treatment methadone is given in small increments, while opioid use is slowly reduced. Eventually, methadone can safely replace heroin or other short-acting opioids. Doctors can then either try to wean the patient off methadone or continue to prescribe methadone as a type of maintenance treatment against withdrawal.

Naltrexone, as an opioid antagonist, is a drug that counteracts the effect of opioids. The drug is commonly used after rehab to prevent relapse.

Buprenorphine (Subutex) was introduced as an alternative to methadone in 2002, but was unpopular due to reported instances of abuse. Indivior developed the mixed opioid agonist-antagonist Suboxone, which combatted this problem.

Dr Reddy's Laboratories (DRL) recently released a generic version of Suboxone after a lengthy court battle with Indivior over patent rights.

Some other agonist-antagonist treatments have also proved effective, like [Orexo's branded buprenorphine and naloxone mix](#), Zubsolv. The drug naloxone is used in isolation for the treatment of overdoses, as a fast-acting opioid antagonist. Opiant Pharmaceuticals developed a nasal spray variant of naloxone, NARCAN, which was approved in 2016.